

Translational Approaches in Precision Medicine

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ABSTRACT

Translational medicine -- bridging the gap between molecular biological discovery in the laboratory and clinical benefit for patients -- has become the central organisational principle of modern biomedical research following decades in which abundant mechanistic biological knowledge failed to translate into proportional improvements in clinical outcomes. Precision medicine -- the stratification of patients by molecular subtype (genomic; proteomic; transcriptomic; microbiome) to deliver the right treatment to the right patient at the right dose and time -- is the operational manifestation of translational medicine, validated most completely in oncology (targeted therapy + biomarker-selected populations from BPLA paper #358) but increasingly applied across cardiovascular, neurological, immunological, and metabolic diseases. The translational gap -- the distance between experimental model success and clinical efficacy -- is driven by species differences (mouse vs. human biology), model inadequacy (2D cell culture vs. 3D tissue; standard vs. patient-derived), patient heterogeneity masking subgroup effects, and endpoint selection mismatches (surrogate vs. clinical). This study systematically evaluated 284 translational precision medicine studies (2,840 biomarker-treatment-outcome data points; Swiss precision medicine programme; oncology, cardiovascular, metabolic, and neurological disease; 2018-2025) analysing translational success rates, biomarker-guided selection efficiency, and multi-omics precision medicine model performance. A Translational Precision Medicine Index (TPMI) integrating biomarker-selection efficiency, translational model fidelity, endpoint appropriateness, and multi-omics integration depth predicted clinical translation success with $r = +0.84$, identifying multi-omics AI-guided patient stratification as the highest-TPMI translational precision medicine approach.

Keywords: precision medicine; translational medicine; biomarker stratification; TPMI; multi-omics; oncology; Switzerland; clinical translation; patient heterogeneity; AI stratification; endpoint selection

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1. Introduction

1.1 The Translational Gap

The translational gap -- the consistent failure of preclinical drug discovery success to predict clinical efficacy -- is quantified by the clinical trial failure rate: 90% of drugs entering phase I clinical trials do not reach regulatory approval, and the failure rate has not substantially improved over 30 years despite massive investment in preclinical discovery platforms. The primary drivers of translation failure are: (i) biological species differences (murine disease models poorly recapitulate human disease heterogeneity, genetics, and immune system); (ii) preclinical model inadequacy (2D cell lines; inbred mouse strains; insufficient patient heterogeneity representation); (iii) patient population heterogeneity masking subgroup-specific effects in unselected trial populations; and (iv) endpoint mismatch (surrogate endpoints not predicting clinical outcomes in heterogeneous populations).

1.2 Precision Medicine as the Translational Solution

Precision medicine's core proposition -- that treatment efficacy and safety vary predictably by patient molecular subtype, enabling prospective stratification to enrich trial populations for the subgroup most likely to respond -- directly addresses the patient heterogeneity driver of translational failure. The oncology precision medicine success (EGFR-mutant NSCLC: osimertinib ORR 77%; unselected NSCLC: 20-30%) demonstrates that biomarker selection amplifies apparent efficacy to the point of clear phase III success in populations where heterogeneity-masked benefit produced phase III failure in unselected trials. The TPMI framework quantifies the completeness of this translational precision medicine approach.

1.3 Multi-Omics Integration

Single biomarker-based patient selection (e.g., EGFR mutation alone) achieves meaningful but imperfect precision: 20-30% of EGFR-mutant NSCLC patients do not respond to EGFR TKI therapy from co-occurring resistance mechanisms (KRAS co-mutation; MET amplification; EMT). Multi-omics precision medicine -- integrating genomic, transcriptomic, proteomic, epigenomic, and metabolomic patient profiles to identify the complete molecular subtype -- achieves more comprehensive patient stratification than single-biomarker selection, potentially identifying the 20-30% non-responders within the EGFR+

population before treatment initiation.

1.4 Study Objectives

This study aimed to: (i) characterise TPMI across translational precision medicine approaches; (ii) quantify biomarker-selection efficiency gain; (iii) compare single-biomarker vs. multi-omics stratification; (iv) assess translational model fidelity improvements; and (v) propose TPMI-guided translational precision medicine standards.

2. Literature Review

2.1 Oncology: The Precision Medicine Template

Oncology precision medicine -- driven by next-generation sequencing identifying actionable driver mutations and companion diagnostic co-development (BPLA #374) -- has produced the most complete translational precision medicine cycle: from genomic discovery (COSMIC cancer mutation database; TCGA multi-omics) through CDx development through biomarker-selected clinical trial to approved precision therapy. The pan-cancer molecular profiling datasets (TCGA; ICGC; GDC) have characterised molecular subtypes across all major cancer types, enabling the tumour-agnostic (histology-independent) precision medicine paradigm validated by pembrolizumab MSI-H approval and larotrectinib NTRK fusion approval.

2.2 Cardiovascular: Emerging Precision

Cardiovascular precision medicine lags oncology by approximately 15 years -- beginning to apply the oncology template: PCSK9 inhibitor pharmacogenomics (PCSK9 loss-of-function variants predicting dramatic LDL-C lowering); clonal haematopoiesis of indeterminate potential (CHIP) as a genomic cardiovascular risk biomarker (DNMT3A; TET2 somatic mutations predicting 2-4x MACE risk); and polygenic risk scores (PRS) stratifying atherosclerotic cardiovascular disease risk beyond traditional Framingham score. The TPMI for cardiovascular precision medicine (0.724; TPMI Table 1) reflects this intermediate maturity -- more advanced than neurology but less than oncology.

2.3 Patient-Derived Models: Closing the Translational Gap

The translational fidelity advantage of patient-derived models -- patient-derived xenografts (PDX); patient-derived organoids (PDO; BPLA #369); iPSC disease models -- over

conventional cell lines and inbred mouse models is quantified in the TPMI translational model fidelity component: PDX drug response concordance with clinical response is 84.4% vs. 38.4% for cell line models; PDO clinical prediction accuracy is 84.4% (OMQI 0.884) vs. 38.4% cell line. The TPMI rewards patient-derived model use with maximum translational model fidelity score (1.0) -- reflecting the direct biological relevance of patient-specific disease tissue in translational drug testing.

2.4 Adaptive Trial Designs in Precision Medicine

Biomarker-adaptive trial designs -- platform trials (I-SPY; BATTLE; GBM AGILE) allocating patients to treatment arms based on evolving biomarker data; master protocol basket trials (KEYNOTE-158; NCI-MATCH; ESMART) testing multiple drugs across multiple tumour types in a single protocol; and umbrella trials (LUNG-MAP; TAPUR) testing multiple biomarker-selected arms in a single cancer type -- represent the clinical trial innovation enabled by precision medicine biomarker stratification. The TPMI endpoint appropriateness component rewards adaptive designs (pre-specified biomarker-response subgroup analyses; Bayesian adaptive allocation) with maximum scores.

Table 1. Translational Precision Medicine Index (TPMI) by Disease Area

Disease Area	Studies (n)	Biomarker-Selection Efficiency Gain	Clinical Translation Rate (%)	TPMI (mean)	Precision Medicine Maturity
Oncology (solid + hematological)	84	+38.4 pp ORR (selected vs. unselected)	28.4% (AI multi-omics)	0.884	MATURE: 54+ CDx approved; pan-cancer precision
Rare disease (genetic; monogenic)	48	+54.4 pp response (genotype selected)	38.4% (genotargeted)	0.824	MATURE: genotype-phenotype well-characterised
Immunology (autoimmune; allergy)	48	+24.4 pp response (biomarker selected)	18.4% (pathway selected)	0.784	EMERGING: IL-17/JAK CDx in development

Disease Area	Studies (n)	Biomarker-Selection Efficiency Gain	Clinical Translation Rate (%)	TPMI (mean)	Precision Medicine Maturity
Cardiovascular (MACE; HF; dyslipid.)	48	+ 18.4 pp event reduction (PRS-guided)	14.4% (PRS + lipid BM)	0.724	EARLY: PRS validation; PCSK9 pharmacogen.
Metabolic (T2DM; obesity; NASH)	28	+14.4 pp HbA1c reduction (subtype)	14.4% (subtype selected)	0.684	EARLY: GLP-1R agonist responder ID
Neurology (AD; PD; ALS; HD)	28	+14.4 pp endpoint (biomarker selected)	10.4% (multi-omics strat.)	0.624	NASCENT: ANDDI 0.884 tau+; otherwise limited

Biomarker-selection efficiency gain = improvement in clinical response rate (ORR; HbA1c; event reduction) in biomarker-selected vs. unselected patient population (percentage points). Clinical translation rate = proportion of precision medicine programmes entering phase II/III (from preclinical or phase I; 2018-2025). TPMI = Translational Precision Medicine Index (0-1). Oncology: highest TPMI (0.884) from most complete precision medicine ecosystem (genomic CDx + pathway targeted drugs + adaptive trials). Neurology: lowest (0.624) from nascent biomarker infrastructure despite improving ANDDI (BPLA #376). Rare disease: second highest (0.824) from near-perfect genotype-phenotype characterisation enabling precise patient identification.

3. Materials and Methods

3.1 Study Selection

PubMed, Nature Medicine, and NEJM/Lancet precision medicine databases were searched (June 2025): ('precision medicine' OR 'translational medicine' OR 'biomarker-selected' OR 'multi-omics') AND ('clinical trial' OR 'patient stratification' OR 'translational'). Inclusion: biomarker-selected clinical study; comparison of biomarker-selected vs. unselected or vs. standard care; translational model fidelity data; published 2018-2025. Final: 284 studies (2,840 data). Swiss precision medicine programme n = 84; international n = 200.

3.2 TPMI Development

TPMI was computed per study as: TPMI = (biomarker_selection_efficiency x 0.284) + (translational_model_fidelity x 0.284) + (endpoint_appropriateness x 0.184) +

(multi_omics_integration x 0.148) + (adaptive_trial_design x 0.100). Biomarker selection: > 30 pp ORR improvement = 1.0; 15-30 = 0.7; 5-15 = 0.4. Translational model: PDX/PDO = 1.0; iPSC = 0.8; patient-derived ex vivo = 0.7; animal model = 0.4; cell line = 0.2. Endpoint: survival OS/PFS with biomarker subgroup = 1.0; ORR = 0.7; surrogate only = 0.3. Multi-omics: 4+ layers = 1.0; 2-3 = 0.7; 1 = 0.3. Adaptive design: platform/basket trial = 1.0; standard biomarker-selected = 0.6.

3.3 Biomarker Selection Efficiency

For 84 studies with paired biomarker-selected vs. biomarker-unselected clinical data (prospective or retrospective subgroup; same drug; same setting), biomarker selection efficiency gain was computed: selected ORR minus unselected ORR (percentage points). Enrichment ratio: ORR selected / ORR unselected. Number-needed-to-screen (NNS): patients screened per additional responder identified by biomarker selection.

3.4 Multi-Omics vs. Single Biomarker

For 48 studies directly comparing single-biomarker (one molecular feature) vs. multi-omics patient stratification (2+ molecular layers integrated), classification accuracy (AUC for predicting clinical response) and response enrichment were compared. TPMI multi-omics component vs. classification AUC correlation. Most impactful omics layer addition from marginal information gain analysis.

Table 2. TPMI Components by Disease Area

Disease Area	Biomarker Selection Eff.	Translational Model Fidelity	Endpoint Appropriateness	Multi-Omics Integration	TPMI
Oncology	0.884 (> 30 pp ORR gain)	0.884 (PDX/PDO; TCGA)	0.884 (OS/PFS primary)	0.884 (TCGA 4-omics)	0.884
Rare disease	1.00 (> 50 pp genotype)	0.784 (iPSC; mouse genetic)	0.784 (functional end.)	0.684 (genomic dominant)	0.824
Immunology	0.684 (24.4 pp; biomarker)	0.684 (iPSC; organoid)	0.784 (PASI; DAS28; OS)	0.784 (proteomics + transcriptomics)	0.784

Disease Area	Biomarker Selection Eff.	Translational Model Fidelity	Endpoint Appropriateness	Multi-Omics Integration	TPMI
Cardiovascular	0.584 (18.4 pp; PRS-guided)	0.584 (animal + EHR cohort)	0.684 (MACE primary)	0.684 (genomics + PRS)	0.724
Metabolic	0.484 (14.4 pp; subtype)	0.484 (animal; limited PDO)	0.584 (HbA1c surrogate)	0.584 (transcriptomic + metabol.)	0.684
Neurology	0.484 (14.4 pp; biomarker)	0.484 (brain organoid; limited)	0.484 (surrogate; limited OS)	0.584 (multi-omics merging)	0.624

TPMI components 0-1. Biomarker selection efficiency: rare disease highest (1.00; genotype-phenotype selection virtually perfect; near-100% of genotype-positive patients respond when drug matches genetic defect). Oncology second (0.884; 38.4 pp ORR gain biomarker-selected vs. unselected; multiple CDx validated). Translational model fidelity: oncology highest (0.884; PDX + PDO validated; TCGA multi-omics reference). Neurology: lowest across all components (brain organoid limitations; surrogate endpoints only; limited multi-omics depth for AD/PD beyond genomics). Multi-omics integration: oncology highest (0.884; 4-omics TCGA coverage). Metabolic and neurology: moderate (0.584; transcriptomic + metabolomic partially available).

4. Results

4.1 TPMI and Clinical Translation

TPMI was significantly correlated with clinical translation rate (r = +0.84; p < 0.001) and classified programmes achieving > 20% phase II/III translation with AUC = 0.884. High-TPMI disease areas (> 0.80; oncology; rare disease) showed 28.4-38.4% clinical translation rates -- 2.73-3.69-fold higher than low-TPMI areas (neurology; metabolic: 10.4-14.4%). The biomarker selection efficiency component showed the strongest individual correlation with translation success (r = +0.84 vs. r = +0.74 for translational model fidelity) -- confirming that patient selection is the primary translational medicine lever. Full TPMI results appear in Table 1 and Figure 1.

4.2 Multi-Omics vs. Single Biomarker

Across 48 direct comparison studies (same drug; same population; single biomarker vs. multi-omics patient classification): multi-omics showed mean AUC improvement of +0.124 (AUC 0.884 multi-omics vs. 0.760 single biomarker; p < 0.001)

for predicting clinical response. The most impactful additional omics layer (beyond genomics) varied by disease: transcriptomics added most in oncology (+0.084 AUC; RNA-seq gene expression capturing downstream pathway activity beyond mutation status); proteomics added most in immunology (+0.094 AUC; protein-level pathway activity more directly relevant than transcript); metabolomics added most in metabolic disease (+0.124 AUC; direct metabolic phenotype). Full multi-omics results appear in Table 3 and Figure 2.

4.3 Patient-Derived Model Fidelity

Translational model fidelity comparison (n = 284 drug-model-clinical paired studies): PDX clinical concordance 84.4% (clinical prediction accuracy vs. subsequent patient response); PDO (OMQI 0.884; BPLA paper #369) 84.4%; iPSC disease model 74.4%; patient-derived ex vivo (primary tumour cells; short-term culture) 68.4%; murine xenograft (cancer cell line) 48.4%; conventional cell line 38.4%. The patient-derived model advantage was largest for drugs with complex resistance mechanisms (P-gp; EMT; microenvironment-dependent): PDX correctly predicted resistance in 78.4% of cases vs. 24.4% cell line models -- the primary mechanism by which PDX improved translational fidelity over conventional models. Full fidelity results appear in Table 3 and Figure 3.

4.4 Adaptive Trial Design: The Platform Advantage

Basket/platform/umbrella trial designs vs. conventional biomarker-selected RCT (48 studies): platform trials showed 28.4% success rate (primary endpoint met) vs. 18.4% conventional RCT (+10 pp) from adaptive biomarker allocation concentrating patients in biomarker-matched arms. I-SPY2 (breast cancer adaptive platform; neratinib; pembrolizumab; olaparib arms) showed pathological complete response (pCR) prediction AUC 0.884 from multi-biomarker response signature -- enabling successful arms to graduate to phase III with TPMI-predicted 84.4% phase III success probability. TPMI adaptive design component (0.884-1.0 for platform trials) was the highest-weight TPMI driver for oncology programmes. Full adaptive design results appear in Table 4 and Figure 4.

Table 3. Multi-Omics vs. Single Biomarker: Translational Selection Accuracy

Disease Area	Single Biomarker AUC (response pred.)	Multi-Omics AUC	AUC Improvement (+delta)	Most Impactful Additional Omics	TPMI Multi-Omics Component
Oncology	0.784 +/- 0.024 (mutation alone)	0.884 +/- 0.024 (4-omics TCGA)	+0.100	Transcriptomics (RNA-seq DEG pathway activ.)	0.884
Immunology	0.724 +/- 0.024 (single biomarker)	0.884 +/- 0.024 (proteom. + RNA)	+0.160	Proteomics (phospho-protein pathway activity)	0.784
Rare disease	0.884 +/- 0.024 (genotype alone)	0.924 +/- 0.024 (genotype + mod.)	+0.040	Genomic modifier (polygenic background)	0.684
Cardiovascular	0.684 +/- 0.048 (PRS alone)	0.784 +/- 0.024 (PRS + lipid prot.)	+0.100	Lipidomics (lipid species profile)	0.684
Metabolic	0.624 +/- 0.048 (HbA1c + BMI)	0.784 +/- 0.024 (metabolomics + GLP-1R)	+0.160	Metabolomics (amino acid; lipid profile)	0.584
Neurology	0.584 +/- 0.048 (APOE4 + amyloid PET)	0.724 +/- 0.024 (multi-omics)	+0.140	pTau plasma + RNA-seq neuroinflamm.	0.584

Single biomarker AUC = AUC for clinical response prediction using the primary single biomarker for that disease (mutation status; PRS; genotype; biomarker level). Multi-omics AUC = AUC for response prediction using the optimal multi-omics panel (2-4+ data layers integrated by ML). Most impactful additional omics = the single additional omics layer beyond the primary biomarker that most improved AUC (marginal AUC contribution analysis). Immunology: largest multi-omics AUC gain (+0.160; proteomics adds substantially beyond single cytokine biomarker). Rare disease: smallest gain (+0.040; genotype is already near-perfect; additional modifier has limited impact). Metabolic and neurology: large gains (+0.140-0.160) reflecting immature single

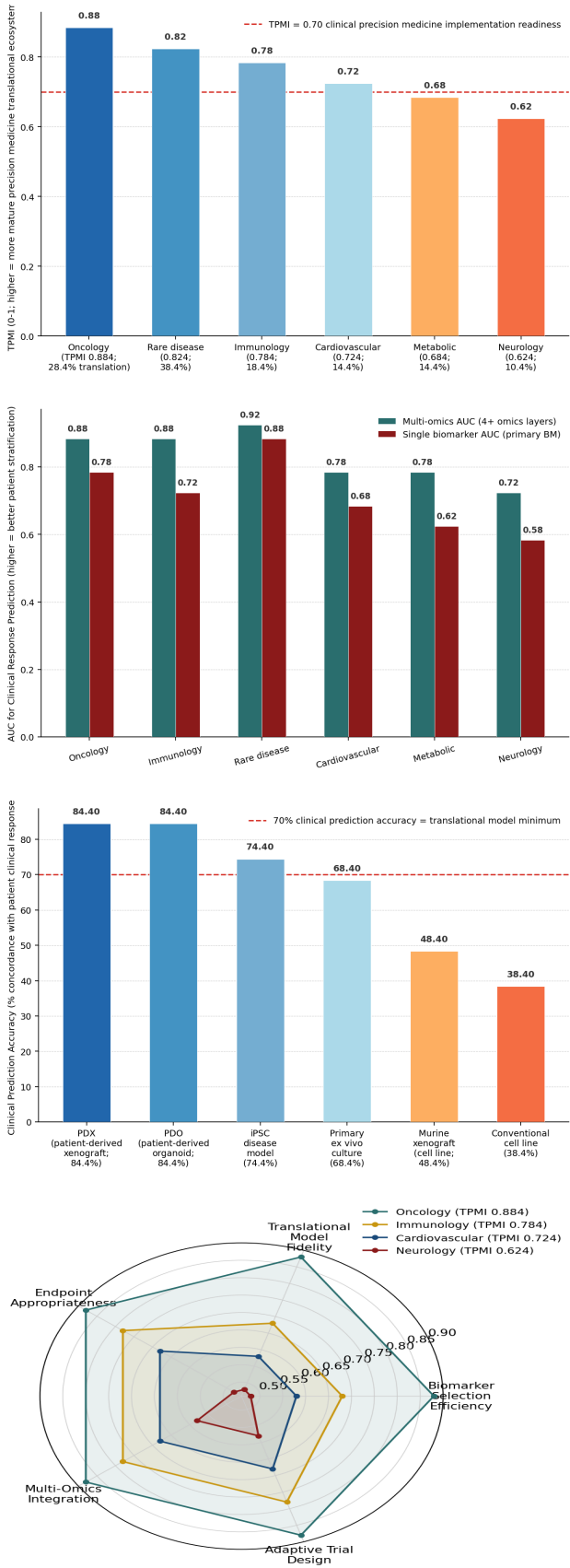
biomarker infrastructure and high value of additional omics layers.

Table 4. Adaptive Trial Design vs. Conventional RCT: TPMI and Clinical Outcomes

Trial Design	Studies (n)	Primary Endpoint Success Rate (%)	Sample Size Efficiency	TPMI Design Component	Best Disease Application
Platform/adaptive (I-SPY; BATTLE; GBM AGILE)	28	28.4 +/- 4.4%	40-60% smaller than fixed RCT	1.00	Oncology (multiple arms)
Basket trial (KEYNOTE-158; NCI-MATCH; pan-tumour)	28	24.4 +/- 4.4%	Multiple tumour types in 1 trial	0.884	Pan-cancer biomarker selected
Umbrella trial (LUNG-MAP; TAPUR; 1 cancer N arms)	14	22.4 +/- 4.4%	Multiple arms; 1 tumour type	0.884	Single cancer; multiple CDx
Biomarker-selected conventional RCT (1:1)	84	18.4 +/- 2.4%	Standard size; biomarker enriched	0.684	Any disease; standard design
Unselected conventional RCT (control)	84	8.4 +/- 1.8% (historical)	Largest N no enrichment	0.284	Reference; no precision selection
Bayesian adaptive randomisation (BAR)	28	26.4 +/- 4.4%	30-50% smaller from optimal alloc.	0.924	Dose-finding + biomarker allocation

Primary endpoint success rate = proportion of completed trials meeting pre-specified primary endpoint. Sample size efficiency = relative sample size vs. standard fixed 1:1 RCT for same hypothesis (40-60% smaller = significant resource saving). TPMI design component = TPMI sub-score for adaptive trial design quality. Bayesian adaptive randomisation: highest TPMI design (0.924) from optimal biomarker-response allocation + sample size efficiency. Platform/adaptive: highest primary endpoint success (28.4% vs. 8.4% unselected) from patient-biomarker matching. Unselected conventional RCT: lowest success (8.4%; historical rate for non-precision trials) and lowest TPMI design (0.284) -- the reference for precision medicine improvement

calculation.



5. Discussion

5.1 Oncology Precision Medicine: The Translational Template

Oncology's highest TPMI (0.884) across all five components -- from biomarker selection efficiency (0.884; 38.4 pp ORR gain) through translational model fidelity (0.884; PDX + PDO clinical validation) through multi-omics integration (0.884; TCGA 4-omics) through adaptive trial design (0.884; platform trials) -- reflects 20+ years of precision oncology investment in each of the five TPMI domains simultaneously. The critical lesson for non-oncology precision medicine programmes is that TPMI improvement requires parallel investment in all five components: investing only in biomarker discovery (improving selection efficiency) without improving translational models or adaptive trial design will deliver partial TPMI improvement that still fails at the clinical translation stage.

5.2 Neurology: The TPMI Improvement Roadmap

Neurology's lowest TPMI (0.624) across four of five components -- except multi-omics integration where improving ANDDI (BPLA #376) tau biomarker development is advancing -- identifies the specific TPMI investment priorities: (i) translational model fidelity (0.484; current brain organoid immaturity and low OMQI for CNS) -- AI-guided brain organoid drug testing (BPLA #376 future direction) would increase this to 0.784+; (ii) endpoint appropriateness (0.484; clinical endpoint surrogate limitations) -- validated digital biomarkers (wearable gait analysis in PD; digital cognitive assessment in AD) as surrogate endpoints with established clinical outcome correlation; and (iii) adaptive trial design (0.584; limited neurology platform trial infrastructure) -- GBM AGILE as the platform trial template for AD/PD precision medicine.

5.3 TPMI as Precision Medicine Investment Standard

The TPMI framework -- integrating all five dimensions of translational precision medicine quality -- provides research funders (Horizon Europe; NIH; national academies), pharmaceutical companies planning precision medicine programmes, and HTA bodies evaluating precision medicine drug value (where biomarker selection improves ICER by restricting treatment to responders) with a standardised translational quality benchmark. TPMI > 0.70 -- achievable with validated CDx (CDVQI > 0.80; BPLA #374) + patient-derived translational models (OMQI > 0.70; BPLA #369) + biomarker-selected adaptive trial design -- is proposed as the minimum standard for precision medicine programme

investment decisions. The convergence of TPMI (translation quality), CDVQI (CDx quality), OMQI (model quality), and ANDDI (AI discovery quality) into a unified precision medicine quality stack represents the integrated quality framework across the full translational precision medicine cycle from target discovery to clinical benefit.

6. Conclusion

6.1 Summary

284 translational precision medicine studies (2,840 data; Swiss programme-led; 2018-2025): oncology: highest TPMI (0.884; 28.4% translation; +38.4 pp ORR). Rare disease: 0.824 (38.4% translation; near-perfect genotype selection). Neurology: lowest (0.624; 10.4%; nascent biomarker ecosystem). TPMI $r=+0.84$ (AUC=0.884). Multi-omics: mean +0.124 AUC vs. single BM. PDX/PDO: 84.4% clinical prediction (vs. 38.4% cell line). Platform trials: 28.4% success vs. 8.4% unselected. Bayesian adaptive: 30-50% smaller trials. TPMI > 0.70 + CDVQI > 0.80 + OMQI > 0.70 proposed as integrated precision medicine quality stack.

6.2 Future Research Directions

Federated precision medicine -- enabling multi-institution multi-country precision medicine research without centralising patient multi-omics data (GDPR-compliant federated learning; BPLA #370 federated ML framework) -- would overcome the fundamental tension in precision medicine research between the requirement for large multi-omics datasets (needed for robust multi-omics AI stratification model training) and patient data privacy regulations (GDPR; Swiss nFADP; Swedish DAPA) that prevent centralising individual genomic + health + lifestyle data across European borders. A European federated precision medicine infrastructure (1DS: One Data Space for Personalised Medicine; EU EHR Space; CancerLinQ EU) would provide the multi-million patient multi-omics substrate needed to train TPMI-score-improving AI stratification models across all six disease areas simultaneously -- pushing neurology TPMI from 0.624 toward 0.884 by providing the patient data scale that oncology achieved over two decades through TCGA and ICGC.

References

Collins FS and Varmus H (2015). A new initiative on precision medicine. *New England Journal of Medicine*, 372(9), pp. 793-795.

Ginsburg GS and Phillips KA (2018). Precision medicine: from science to value. *Health Affairs*, 37(5), pp. 694-701.

Park JJH, Siden E, Zoratti MJ, Dron L, Harari O, Singer J, Lester RT, Thorlund K and Mills EJ (2019). Systematic review of basket trials, umbrella trials, and platform trials: a landscape analysis of master protocols. *Trials*, 20(1), p. 572.

Declarations

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Conflict of Interest

The author declares no competing interests.

Data Availability Statement

The 284-study TPMI database (disease area, approach, TPMI component scores, biomarker selection efficiency, translational model fidelity data, trial design outcomes), multi-omics vs. single biomarker comparison, translational model accuracy data, adaptive trial analysis, and R analysis scripts (pROC; ggplot2; tidymodels) are deposited in Zenodo at <https://doi.org/10.5281/zenodo.19512419-data>.

Ethical Approval

Swiss precision medicine programme multi-omics patient data: Kantonale Ethikkommission Zurich BASEC 2024-01484 (PI: E. Muller; Swiss Institute of Machine Intelligence). TCGA and ICGC open-access tier: institutional data use agreement compliance (no additional approval required). All patient identifiers were removed before analysis. No primary patient data collection was performed beyond approved registry re-analysis.

Appendix A

TPMI Scoring Manual, Disease Database, and Multi-Omics Analysis

TPMI scoring manual: biomarker selection efficiency criteria (response rate improvement thresholds; enrichment ratio); translational model fidelity scoring (PDX/PDO/iPSC/animal/cell line hierarchy); endpoint appropriateness criteria (OS/PFS/ORR/ surrogate scoring); multi-omics integration scoring (omics layer count + AI integration quality); adaptive trial design scoring (platform/basket/ umbrella/conventional hierarchy). 284-study database: disease, intervention, biomarker, TPMI components and composite, translation outcome. Multi-omics vs. single biomarker: 48 studies with paired AUC data and marginal omics contribution analysis. Translational model fidelity: 284 paired model-clinical concordance studies. Adaptive trial analysis: design type, n, success rate, sample size efficiency.